been added, and claim 72 has been canceled. Therefore, claims 60, 66-71, and 73-96 are currently pending. The amendment to the specification corrects a formality and perfects Applicants' priority claim. The claim for priority was made in the transmittal letter as filed and in the Declaration. Support for the amendments and new claims is found in the specification and claims as originally filed. Particular support for the amendments and new claims is discussed in the preliminary amendment filed May 24, 2001, or is explained below. As such, these amendments introduce no new matter, and Applicants respectfully request their entry.

I. Priority

Applicants thank the Examiner for bringing to their attention the inadvertent lack of recitation of the appropriate priority data as the first line of the application. The amendment to the specification corrects this defect, and properly claims benefit of priority of the applications identified in the transmittal letter and the originally filed declaration. Reconsideration is respectfully requested in view of the amendment.

II. Rejection Under 35 U.S.C. § 102(b)

The Office has maintained the allegation that Cravioto et al., *J. Infect. Dis.* 163: 1247-55 (1991), anticipates Applicants' invention. Applicants respectfully traverse this rejection.

As an initial matter, the phrase "enriched or purified intimin" and its relation to Cravioto et al. was discussed in the interview of May 15, 2001 (see Interview Summary mailed May 17, 2001, Paper No. 29), which noted: "Claim limitation drawn to administration of enriched or purified intimin would define over this reference."

While the Office Action quotes the specification at page 6, lines 3-7, its use of this quote is misleading because it is taken out of context. That quotation simply provides background information by pointing out that *Shigella* and *Salmonella*, like EHEC, infect gastrointestinal tissue and produce antigens.

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1300 I STREET, N. W.
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Applicants traverse this rejection first because one of ordinary skill in the art would understand that "enriched or purified" refers to intimin wherein the concentration has been increased over the concentration initially present in the original source. It is this definition of "enriched or purified" that Applicants intend to be used in construction of the claims. Indeed, Applicants are entitled to be their own lexicographers. M.P.E.P. § 2111.01. Support for this definition is found in the specification, which illustrates several methods of enriching and purifying intimin from an original source. (See, for example, page 7, line 12 to page 8, line 8.) The "enriched or purified intimin" does *not* include the intimin released from bacteria naturally present in a host in the course of a disease-producing infection in that same host.

Second, the Office states that "'enriched' is being viewed to include enriched expression of intimin by the pathogen under disease producing conditions." (Office Action at page 4.) Applicants note that a pathogen does not increase, or enrich, the concentration of its own intimin during infection in the body.

Finally, regarding "administering," Applicants note that in a claim reciting a therapeutic method for providing passive immune protection, one of ordinary skill in the art would not believe administration would include a disease-producing and life threatening infection. Administering is defined as "to give or apply in a formal way" or "to apply as a remedy." *American Heritage Dictionary*, 3rd. Ed. Applicants respectfully note that this fails to include disease producing infection. Applicants intend that administration be defined to include all methods of giving, applying, and introducing enriched or purified intimin from sources external to the host to which intimin is being administered.

III. Rejection Under 35 U.S.C. § 103(a)

The Office maintained the rejection of claim 60 as allegedly obvious in view of Dougan et al., U.S. Pat. No. 5,747,293. The Office stated at pages 7-8 of the Office Action that Applicants' submission of commercial success and unexpected results are unpersuasive,

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1300 I STREET, N. W.
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contending that the license does not indicate commercial success of a product and that the data presented in the Dean-Nystrom abstract is not commensurate in scope with the claim.

Applicants submit with respect to the license that the commercialization of biotechnology methods and products is often exceedingly long and requires the approval of one or more regulatory agencies. The instant license demonstrates commercial success because the licensee has recognized with its pocketbook the value of the disclosed technology at an early stage and will absorb much of the very high costs associated with commercial development and regulatory approval of the method. Applicants submit that the purpose of a license is to bring the subject of an invention to market. Thus, by definition, the license of a claimed technology at the stage of development of the claimed technology is the very essence of commercial success of a product.

The Preliminary Amendment of May 24, 2001, at pages 9-10, describes the Dean-Nystrom experiment. Applicants acknowledge that the hosts and patients of Applicants' claims comprise several animals, including humans; however, Applicants cannot ethically perform experiments like those of Dean-Nystrom on humans. One cannot ethically determine if humans ingesting milk from vaccinated animals are protected from EHEC symptoms by inoculating the humans with EHEC as Dean-Nystrom did with piglets. However, the pig model was chosen for the Dean-Nystrom experiment largely because the pig immune system it is a *good and accepted model* in the art for the human immune system.

For example, the attached 1994 abstract by Butler and Brown (Exhibit A) points out that the immunoglobulin genes in pigs are similar in structure and expression pattern to those of humans and states that the swine is an attractive model for human immunootogeny. Thus, one skilled in the art would expect that if the Dean-Nystrom experiment were conducted on humans that similar results would be achieved. Indeed, the Federal Circuit has repeatedly maintained that a showing of unexpected results for a species in a claimed genus is sufficient to rebut a prima facie case of obviousness throughout the entire scope of the claim when one skilled in the art can reasonably conclude that similar results would be obtained for other members of the genus. *See, e.g., In re Chupp*, 816 F.2d 643, 646, 2 U.S.P.Q.2d 1437, 1439 (Fed. Cir. 1987); *In*

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FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
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re Clemens, 622 F.2d 1029, 1036, 206 U.S.P.Q. 289, 296 (CCPA 1980). The Office also contends that the Dean-Nystrom abstract is not applicable to non-colostral antibodies with titers lower than 100,000. Applicants submit that it would be difficult to test different sources and titers because this experiment relies on the natural physiological responses of the sows to the vaccine.

Moreover, the Office has provided no credible factual evidence to support its assertion that the Dean-Nystrom abstract applies only to pigs with colostral antibodies of titers greater than or equal to 100,000. The burden is on the Office to provide a credible factual basis consistent with the substantial evidence standard of *In re Zurko*, 258 F.3d 1379, 59 U.S.P.Q.2d 1693 (Fed. Cir. 2001), showing why the testing of a specific species with colostral antibodies is insufficient to rebut the prima facie case. Indeed, the Federal Circuit has recently pointed out that the Office "cannot rely on conclusory statements" in establishing a prima facie case of obviousness, "but must set forth the rationale on which it relies," and that "[t]his precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Lee*, No. 00-1158, Slip op. at 6, 8, 11 (Fed. Cir. Jan. 18, 2002) (citations omitted).

IV. Rejection Under 35 U.S.C. § 112, First Paragraph

The Office rejected claims 72-73, 75, 78-79, and 82 as allegedly nonenabled for recitation of "butchering" and "breeding said at least one animal," and further alleging that these terms constitute new matter. Applicants respectfully submit that these rejections are now moot because: 1) claim 72 has been canceled, and 2) claim 73 has been rewritten to recite an independent claim to a method of providing a safer food source consistent with the December 19, 2001, Interview Summary.

V. Rejection Under 35 U.S.C. § 112, Second Paragraph

The Office rejected claims 66, 68-75, 78-79, and 82 as allegedly indefinite for recitation of various terms addressed individually below.

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FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
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Claim 66 is rejected for recitation of an animal that is "a wildlife." Applicant notes that the instant invention is broad enough to include administration to *any* mammal. Thus, this dependent claim merely recites a specific subset of the "wildlife and laboratory animals" disclosed in the specification. (Specification at pages 18-19.) The *American Heritage College Dictionary*, 3rd Ed., defines wildlife as "[w]ild animals and vegetation, esp. animals living in a natural undomesticated state." Applicants respectfully believe that the term "wildlife" is clear on its face and submit that this rejection is not commensurate with the standard of examination under section 112, which requires only that the claims define the patentable subject matter with *reasonable* clarity and precision. (M.P.E.P. § 2173.02.) Thus, Applicants respectfully request reversal of this rejection.

Claims 68 and 69 were rejected for recitation of a "nursing animal." Applicants have clarified this term by replacing it with "a milk-producing animal" in order to make it clear that the nursing animal is the animal producing milk, i.e., an animal which produces colostrum or milk.

Claim 70 was rejected for recitation of "an animal." This term has been deleted as redundant.

Claims 72 and 73 were rejected for recitation of "butchering." Applicants have obviated this rejection by deleting claim 72 and rewriting claim 73 to recite a method for providing a safer food source, wherein one step comprises "preparing said food animal as a food source for human consumption."

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
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Please grant any additional extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____
Allen R. Jensen
Reg. No. 28,224

Date: January 28, 2002

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
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APPENDIX TO AMENDMENT OF JANUARY 28, 2002

Version with Markings to Show Changes Made

Amendments to the Specification

Please insert the following paragraph at the beginning of the specification:

This application claims priority to Provisional Application Serial No. 60/015,657, filed April 19, 1996, and Provisional Application Serial No. 60/015,936, filed April 22, 1996.

Amendments to the Claims

60. (Twice Amended) A method for providing passive immune protection to a patient in need thereof comprising:

[generating anti-intimin antibodies through administration of enriched or purified intimin protein to a host; and] administering enriched or purified intimin protein to a host to generate anti-intimin antibodies; and

administering an amount of the generated anti-intimin antibodies from [said] the host to the patient effective to provide passive immune protection to the patient;

wherein the anti-intimin antibodies block binding of enterohemorrhagic *E. coli* to a mammalian cell.

66. (Once Amended) The method of claim 60, wherein [said] the host is an animal chosen from at least one of a domesticated animal, wildlife, and a laboratory animal.

67. (Once Amended) The method of claim 66, wherein [said] the host animal is a cow, pig, rabbit, or mouse.

68. (Once Amended) The method of claim 67, wherein [said] the host animal is [at least one of] a [pregnant animal and a nursing] milk-producing animal.

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& DUNNER, L.L.P.
1300 I STREET, N. W.
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69. (Once Amended) The method of claim 68, wherein [said] the patient is an offspring of [said] the [at least one pregnant animal and a nursing] milk-producing animal.

70. (Once Amended) The method of claim 67, wherein [said] the patient is [an animal and] a newborn.

73. (Once Amended) [The method of claim 66] A method of providing a safer food source, comprising:

[generating anti-intimin antibodies through administration of enriched or purified intimin protein to a food animal;] administering enriched or purified intimin protein to a first food mammal to generate anti-intimin antibodies;

administering an amount of the generated anti-intimin antibodies from [said] the first food [animal] mammal to a second food [animal] mammal, wherein [said] the amount of the generated anti-intimin antibodies is effective to provide passive immune protection to the second food [animal] mammal, and wherein the anti-intimin antibodies block binding of enterohemorrhagic *E. coli* to a mammalian cell; and [wherein said host is an animal, further comprising butchering of said host animal]

preparing [said] at least one of the first and the second food [animal] mammals as a food source for human consumption.

74. (Once Amended) The method of claim [68,] 73, wherein the first food mammal is a milk-producing mammal, and further comprising administering the amount of the generated anti-intimin antibodies directly from the milk-producing [pregnant] milk-producing [animal] mammal to its offspring.

75. (Once Amended) The method of claim 74, further comprising birthing [said] the offspring, and [butchering] preparing at least one of [said] the offspring and [said] at least one of the first and second [host animal] food mammals as a food source for human consumption.

76. (Once Amended) A method for providing a safer food source, by providing [an animal] a food mammal with protection from enterohemorrhagic *E. coli* infection comprising:

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1300 I STREET, N. W.
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[generating anti-intimin antibodies through administration of enriched or purified intimin protein to a host] administering enriched or purified intimin protein to a host to generate anti-intimin antibodies; and

administering an amount of the generated anti-intimin antibodies from said host to the food [animal] mammal effective to provide passive immune protection to the food [animal] mammal;

wherein the anti-intimin antibodies block binding of enterohemorrhagic *E. coli* to a mammalian cell, and wherein the safer food source is derived from the food mammal, and the food [animal] mammal is chosen from at least one of a domesticated [animal,] mammal and wildlife[, and a laboratory animal].

77. (Once Amended) The method of claim 76, wherein [said animal] the food mammal is at least one of a cow, pig, and rabbit[, or mouse].

78. (Once Amended) The method of claim [77] 76, further comprising [butchering] preparing said at least one food [animal] mammal as a food source for human consumption.

79. (Once Amended) The method of claim [77] 76, further comprising breeding said at least one food [animal] mammal.

80. (Once Amended) The method of claim [77] 76, wherein [said animal] the food mammal is [at least one of] a [pregnant animal or a nursing] milk-producing animal.

81. (Once Amended) The method of claim 76, wherein [said animal] the food mammal is a cow or a calf.

82. (Once Amended) The method of claim 81, further comprising [butchering] preparing [said] the cow or calf as a food source for human consumption.

84. (Once Amended) The method of claim 73, wherein the injection is [at least one of] intraperitoneal, intravenous, subcutaneous, [and] or intramuscular.

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1300 I STREET, N. W.
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85. (Once Amended) The method of claim [77] 76, wherein the administration of the enriched or purified intimin protein is via injection.

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FARABOW, GARRETT,
& DUNNER, L.L.P.
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1: Vet Immunol Immunopathol 1994 Oct;43(1-3):5-12

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The immunoglobulins and immunoglobulin genes of swine.

Butler JE, Brown WR.

Department of Microbiology, University of Iowa, Iowa City 52242.

The historical works describing the characterization of swine immunoglobulins are reviewed. The three major isotypes, IgM, IgA and IgG, have been recognized for 25 years and their concentrations in various body fluids, the location of the plasma cells throughout the body which synthesize them and their transport into lacteal secretions and absorption by the gut of the newborn piglet, have been studied by many investigators. Swine like humans, have both kappa and lambda light chains and their frequency of expression is similar to that of humans. Various investigators have provided immunochemical evidence for IgG subclass and allotype diversity, although until the recent advent of molecular biology, the complete sequence of any swine immunoglobulin was unknown. Molecular genetic studies reveal single copies of C alpha and C epsilon but as many as eight copies of C gamma. The sequences of five IgG subclasses, IgG1, IgG2a, IgG2b, IgG3 and IgG4, are now available as well as the sequence and genomic organization of C alpha and the sequence of C mu. Swine CH genes all appear to belong to a single small family very similar to human VHIII. Especially interesting is the high degree of similarity among human and swine Ig genes despite the distinct phylogenetic relationship of these species. The rapid expansion of knowledge and technology in the field of molecular biology, together with the attractiveness of the swine as a model for immunoontogeny, in which the influences of both maternal regulatory factors and intestinal gut flora can be experimentally controlled, promises the beginning of an exciting area in swine immunology.

Publication Types:
- Review
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